Prognosis of cancer in persons with infrequent consultations in general practice: a population-based cohort study

Short title: GP consultation frequency and cancer prognosis

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This study is the first to investigate a potential association between cancer patients' usual consultation frequency in general practice and the prognosis of cancer. Patients who usually consult their GP rarely are more likely to be diagnosed with advanced cancer and to die within the first year after the cancer diagnosis. Part of the deficit in cancer survival in Denmark may be attributable to subgroups in the population who tend to consult general practice rarely.

Abbreviations used in manuscript:

GP: general practitioner; DCR: Danish Cancer Registry; TNM: Tumour Node Metastasis; PRN: personal registration number; OECD: Organisation for Economic Cooperation and Development; ISCED: International Standard Classification of Education; CCI: Charlson Comorbidity Index; ICD-10: International Classification of Diseases, 10th revision; CI: confidence intervals; HR: hazard ratio; OR: odds-ratio

Abstract

Cancer survival rates are lower in Denmark than in comparable European countries. This may partly be attributable to subgroups of cancer patients who seek medical attention at late disease stages. It is unknown if differences in usual (i.e. customary) consultation frequency in general practice are associated with cancer prognosis.

We aimed to estimate the cancer prognosis of cancer patients stratified by their usual consultation frequency in general practice.

We performed a population-based cohort study including 123,943 incident cancer patients aged 50-89 years diagnosed in Denmark in 2009-2013. We estimated associations between the patient's usual general practitioner (GP) consultation frequency 19-36 months before the cancer diagnosis and all-cause mortality by using hazard ratios (HR), estimated by Cox proportional hazards regression. We also estimated the associations between the patient's usual GP consultation frequency and tumour stage, by using logistic regression estimates of odds ratios (ORs).

Patients who usually did not see their GP (non-consulters) had higher all-cause mortality (HR=1.39 (95% CI: 1.33-1.44)) compared to patients who usually saw their GP three to five times during an 18 months period (average consulters). Non-consulters had higher odds of having distant tumour stage (OR=1.46 (95% CI: 1.38-1.57)) than average consulters. Similar, yet less strong, patterns were seen among patients with low usual GP consultation frequency, yet not statistically significant for all cancer types.

In conclusion, the association between usual GP non-consultation and cancer prognosis is a combination of at least two things: a mechanism through more advanced tumour stage and other independent factors.

Introduction

The prognosis of cancer patients has been shown to vary internationally.(1-3) Poorer short-term cancer survival is seen in Denmark and England compared with Finland, Norway, and Sweden.(4) Several studies indicate that Danish cancer patients tend to be diagnosed and treated at more advanced disease stages than cancer patients in Norway and Sweden.(5-9) The underlying mechanism is unknown, but a contributory factor could be that some patients delay seeking medical care. As tumours generally grow exponentially, early diagnosis (i.e. early in the tumour's lifespan) is a crucial factor. (10) After decades of conflicting results on the prognostic impact of the time to diagnosis, (11-16) recent evidence suggests that increasing mortality is seen with longer time to diagnosis. (17-20) Therefore, it is vital that patients promptly seek medical advice when symptoms of potential disease are experienced.(11)
The poor cancer survival in Denmark and England have been suggested to be partly attributable to a sub-group of patients who do not seek medical advice until they have developed advanced and fatal cancer.(1)

Patients with undiagnosed cancer tend to increasingly consult their general practitioner (GP) several months before the cancer diagnosis.(21-24) Their consultation pattern thus seems to be influenced by symptoms related to the cancer disease.

Danish residents can consult their GP in several ways: by face-to-face consultation, phone, or email. Danes consult their GP 5-7 times on average per year, but eight percent of Danish residents aged 60 years or older have not consulted their GP at all during the most recent 12 months.(25) Danish GPs are gatekeepers to the rest of the healthcare system and serve as the first point of contact for medical advice. This organisation offers a unique possibility to investigate if differences in the usual GP consultation frequency are associated with the prognosis after diagnosis of cancer.

The aims of this study were to quantify the size of different sub-groups of Danish cancer patients on the basis of their usual consultation pattern in general practice and to estimate their prognosis and distribution of cancer stage.

Material and methods

We performed a population-based cohort study of incident cancer patients who were diagnosed in 2009-2013 in Denmark.

Setting

The 5.6 million residents in Denmark have free access to medical care in the tax-funded healthcare system. Around 98% of the Danish population are listed with a general practice, which they can consult for primary medical care. The GP is the gatekeeper to secondary healthcare, except for emergencies, ear-nose-throat specialists, and eye specialists, who can be accessed directly.(26)

Study population

The cancer cohort was identified in the Danish Cancer Registry (DCR), which holds information on the date of diagnosis and the tumour characteristics of all cancers diagnosed in Denmark.(27) We identified all first-time cancer patients aged 50-90 years who were diagnosed from 1 January 2009 to 31 December 2013. Patients were eligible if they had no previous cancer diagnosis (apart from non-melanoma skin cancer), had a valid civil registration number (i.e. not foreigners treated in Denmark), had been living in Denmark during the 36 months preceding diagnosis, and were listed with a Danish general practice.

The general practice affiliation for each participant was retrieved from the Patient List Register, which is an administrative database that contains information on which general practice each citizen is registered with at any given time.

Outcomes

The primary outcome was all-cause mortality based on the survival time of each patient from the date of diagnosis. Information on death and emigration was obtained up to 31 December 2014 from the Danish Civil Registration System.(28) The date of diagnosis was obtained from the DCR and corresponds to the date of first contact (admission date) with the hospital department at which the cancer diagnosis was first registered. If the patient was diagnosed by a private practicing specialist, the date of diagnosis was defined as the date of the clinical diagnosis.(29)

The secondary outcome was tumour stage. Data was obtained from the DCR and was based on the TNM staging system. We categorised tumour stage for colorectal, lung, breast, prostate, malignant melanoma, and bladder cancers using established cancer-specific algorithms to categorise tumours as either: local, regional, distant, or unknown.(30-35) TNM staging information for the remaining cancers was categorised using the following principle: local (no positive lymph nodes or metastasis), regional (positive lymph nodes), distant (metastatic cancer), and unknown.

Exposure

The primary exposure in the study was the patient's usual (i.e. customary) consultation pattern in general practice. This was defined as the number of daytime face-to-face consultations with a GP, including home visits, in the period 19-36 months prior to the date of cancer diagnosis. Data on consultations with general practice was extracted from the Danish National Health Service Register, which holds information on all contacts and services provided by general practice for remuneration purposes.

To categorise the usual consultation frequency in general practice accurately, we compared the consultation pattern among the cancer patients with a 1:10 sex- and age-matched comparison cohort. The comparison cohort was identified in the Danish Civil Registration System, which holds information on all citizens in Denmark, including their personal registration number (PRN).(28) Based on this, we categorised the cancer patients' usual consultation frequency into seven categories according to the number of face-to-face consultations during the 19-36 months prior to the date of their cancer diagnosis.

Covariates

We collected demographic and socioeconomic information from Statistics Denmark. Marital status was categorised into "married" (married or registered partnership), "widowed and divorced" (widowers, divorcees and annulled partnerships), or "single" (never married or registered partnership). Data on taxable income was extracted for the calendar year preceding the index date to eliminate the risk of influence from the cancer diagnosis on income. Income was categorised into tertiles of the OECD-modified scale. The highest attained level of education was categorised according to the International Standard Classification of Education(36) into "basic" (ISCED levels 1-2), "short" (ISCED levels 3-4), and "long"(ISCED levels 5-6). Patients with missing information on educational level were assigned "basic" educational level as these are most often uneducated.(37) The Charlson Comorbidity Index (CCI) was used to account for comorbidity.(38) A CCI score was calculated on the basis of diagnoses registered in the Danish National Patient Register in the 10-year-period preceding the 18 months prior to the patient's cancer diagnosis. We computed the total CCI score for each patient and grouped levels of comorbidity into "none" (CCI score = 0), "moderate" (CCI score = 1–2), and "high" (CCI score ≥ 3).

Statistical analyses

Analyses were stratified on four major types of cancer according to the International Classification of Diseases, 10th revision (ICD-10): colorectal (C18-C20), lung (C34), female breast (C50), prostate cancer (C61), and a fifth category containing all other cancer types. The analyses were performed for each sex separately as gender differences are known to exist in the use of general practice.

The consultation pattern between the cancer cohort and the comparison subjects was compared by calculating monthly (mean) rates and rate ratios with corresponding 95% confidence intervals (95% CIs) using a negative binominal regression model with robust variance estimation.

We used Cox proportional hazards regression to quantify the relative hazard of death from any cause in relation to the patients' usual consultation frequency. All analyses were adjusted for age (linear and second order terms), sex (binary), marital status (categorical), educational level (categorical), income (categorical), and CCI score (categorical) of the individual patient. In the analysis of all cancers combined, we also adjusted for main type of cancer (colorectal, lung, female breast, prostate, and other cancer) as a categorical variable. The analyses focused on the one-year follow-up time after the cancer diagnosis. Patients surviving beyond one-year follow-up were censored at the one-year time point.

We used logistic regression to analyse the association between the patient's usual consultation pattern and the tumour stage. Analyses were adjusted for the same covariates as outlined above. Missing data on tumour stage is a well-known concern in the DCR and is dependent on sex, age, cancer type, and CCI score. (30-35;39) We examined the distribution of missing tumour stage by all variables used in the model to investigate if multiple imputation was feasible. Multiple imputation of missing values for tumour stage was conducted by using a multivariate model with one-year vital status, sex, age, marital status, educational level, income, CCI, and cancer type as predictive values. We imputed twenty datasets in a chained sequence and used Rubin's formula to combine the outcomes from the imputed datasets.

Data was analysed using the statistical software Stata 14.0 (StataCorp LP, TX).

Results

We identified 123,943 eligible incident cancer cases and 1,239,424 age- and sex-matched comparison subjects. The cancer cases had slightly higher comorbidity scores than the comparison subjects, mainly for lung cancer (Table A1, Appendix). The cancer cases consisted of 17,138 (13.8%) colorectal cancers, 17,861 (14.4%) lung cancers, 18,396 (14.8%) breast cancers, 19,348 (15.6%) prostate cancers, and 51,200 (41.3%) other cancer types (Table 1).

Usual use of general practice

A stable usual use of general practice was seen for both cancer patients and comparison subjects in the 19-36 months prior to diagnosis, although fewer cancer patients had a low GP use compared to the comparison subjects (9.3% and 10.2%, respectively) (Table A1, Appendix). During this period, 9% of cancer patients (8% women, 11% men) did not have any face-to-face contact with their GP (non-consulters), and 23% of cancer cases consulted their GP 3-5 times (average consulters)(Table 1).

Mortality according to usual GP consultation frequency

At one-year follow-up, 33,761 (27%) of the cancer patients had died (26% of women, 29% of men). The proportion of patients who died during the first year varied according to sex and type of cancer, ranging from 4% for female breast cancer patients to 64% for male lung cancer patients (Table 1).

The proportion of deaths was 30% among the patients who had not consulted their GP; 24% among the patients who had consulted their GP two to five times, and 34% among the patients who had consulted their GP more than 15 times (Table 2). The pattern of deaths according to usual GP consultation frequency was similar for both women and men separately, but higher death rates were found for men in all groups (data not shown).

Unadjusted mortality was associated with usual GP consultation frequency, resulting in a concave curve, with the pole around 3-9 consultations with a GP. After adjustment, the association changed to a “hockey stick” curve (Figure 1) with a hazard ratio (HR) of 1.39 (95%CI: 1.33-1.44) in the group of non-consulters compared to average consulters (three to five consultations) during the period 19-36 months before their cancer diagnosis (Table 2). Patients with one or two GP consultations during the same period had intermediate HRs of 1.15 (95%CI: 1.10-1.20) and 1.06 (95%CI: 1.01-1.11), respectively (Table 2).

For specific cancers, the hazard ratios among non-consulters ranged from 2.54 (95%CI: 1.99-3.24) among breast cancer patients to 1.30 (95%CI: 1.23-1.38) among patients with other cancer types. All cancer types investigated had the same overall pattern although with varying HRs, ranging from 1.07 (95%CI: 0.93-1.22)

for colorectal cancer patients to 1.41 (95%CI: 1.08-1.83) for prostate cancer patients (Table 2). The patterns were similar for males and females.

Tumour stage according to usual GP consultation frequency

Twenty percent of the patients were diagnosed with distant cancer, ranging from 4% for breast cancer patients to 58% for male lung cancer patients. Missing data on tumour stage was encountered for 26% of patients, with variations across cancer types (Table 1, Table A2, Appendix). The proportion of distant cancers diagnosed among patients with non-missing tumour stage was 25% for non-consulters and 20% in the remaining patients (data not shown). The pattern of distant tumour stage according to usual GP consultation frequency was similar for both women and men, but with slightly higher proportion of distant cancers for men than women (data not shown).

Low usual GP consultation frequency was associated with distant tumour stage (Table 3). The odds of having distant tumour stage was 1.46 (95%CI: 1.38-1.57) times higher in non-consulters than in average consulters. Patients with one or two GP consultations during the same period had ORs of 1.14 (95%CI: 1.07-1.22) and 1.11 (95%CI: 1.05-1.18), respectively.

For specific cancers, the ORs of having distant tumour stage among non-consulters varied from 3.52 (95%CI: 2.74-4.53) among breast cancer patients to 1.28 (95%CI: 1.17-1.40) among patients with other cancer types than colorectal, lung, breast, or prostate cancer. The same pattern was observed for all cancer types investigated with ORs ranging from 1.06 (95%CI: 0.92-1.22) for colorectal cancer patients to 1.53 (95%CI: 1.22-1.88) for prostate cancer patients (Table 3).

Mortality according to usual GP consultation frequency conditioned on tumour stage

After adjustment for tumour stage at diagnosis, the association between usual GP consultation frequency and mortality attenuated. However, the same pattern was observed as in the fully adjusted model without tumour stage (Table A3, Appendix), with a HR of 1.28 (95%CI: 1.23-1.34) among non-consulters compared to average consulters. For specific cancers, the hazard ratios among non-consulters ranged from 1.60 (95%CI: 1.25-2.04) among breast cancer patients to 1.23 (95%CI: 1.09-1.38) among colorectal cancer patients. The same pattern was observed for all cancer types investigated although with varying HRs (Table A2, Appendix).

Discussion

Principal findings

This analysis of mortality and tumour stage among more than 120,000 cancer patients in Denmark shows that low usual consultation frequency in general practice is associated with a higher risk of being diagnosed with distant tumour stage and a higher risk of dying in the first year after a cancer diagnosis. The association was strongest for patients who did not consult their GP during the 19-36 months before their diagnosis. Adjusting for age, comorbidity, and socioeconomic position explained the poorer prognosis among patients with high consultation frequency in general practice, but it did not explain the poor prognosis among patients with low usual GP consultation frequency. This indicates that the findings may be explained by differences in healthcare-seeking behaviour.

Strengths and limitations

The strengths of this study include the population-based design, which was permitted by the uniformly organised healthcare system in Denmark, the identification of cancer cases in the DCR, and the complete follow-up through national population-based registries. This reduced the risk of selection and information bias. Furthermore, the large study population provided high statistical precision.

Another major strength was the stable and comparable consultation rates in general practice between the cancer patients and the sex- and age-matched comparison subjects. The risk of misclassifications concerning the usual GP consultation frequency among the patients use was thereby minimised. Additionally, the grouping of cancer patients by number of contacts reflects the true usual GP consultation pattern.

A potential limitation was that we included only face-to-face contacts. Some patients may prefer telephone consultations, and we have underestimated the total number of contacts between the patients and the GP. However, from a clinical perspective, the number of face-to-face contacts during more than 1.5 years before the cancer diagnosis is a strong indicator of the usual healthcare-seeking behaviour, even without considering other types of contacts that are more trivial.

The study was based on national population-based registries, and we were not able to adjust for potential confounders such as smoking, alcohol consumption, and physical fitness. As these factors are strongly associated with income and educational level, (40;41) a part of their potential confounding effect has already been accounted for. Thus, we believe that the possible effect of e.g. alcohol consumption or smoking cannot fully explain the observed associations.

Despite its high specificity, the Charlson Comorbidity Index (CCI) does not measure comorbidity as precise as clinical data.(42) Furthermore, the CCI score requires that the patient has actually been in contact with a hospital. Consequently, the CCI score might be too low in the patient groups with low levels of GP consultations. Nevertheless, we observed almost no changes in the estimates for the outcomes of interest when we adjusted for comorbidity, which indicates that the impact is negligible.

Tumour stage is likely to be misclassified due to missing data on tumour stage in the DCR. (39) We used well-established algorithms to produce comparable tumour stage information. (30-35) Our complete case analysis and the analysis using multiple imputation of missing data on tumour stage gave identical results, which makes potential bias due to missing data on tumour stage unlikely.

Misclassification of tumour stage in the DCR cannot be ruled out. (27) Thus, residual confounding from tumour stage will be at play in the sub-analysis of mortality according to usual GP consultation frequency when adjusted for tumour stage. Therefore, these results should be interpreted with caution.

Comparison with relevant literature and interpretation

Direct comparison with other studies of the association between consultation frequency in general practice and mortality is not possible due to the absence of similar studies. Nevertheless, studies measuring continuity of care have reported an association between higher continuity of care in primary care and lower mortality.(43-45) In line with our findings, Wolinsky et al have reported that patients consulting primary care have lower likelihood of early death than non-consulting patients .(45) Similarly, cancer patients diagnosed with colorectal cancer through an “emergency route” who has a poorer prognosis are less likely to consult their GP in the 24-36 months prior to their diagnosis.(46;47)

Lack of evidence is also seen on the association between usual healthcare-seeking and tumour stage. A French study on head and neck cancers found that patients consulting their GP during the last year before a cancer diagnosis had a lower risk of being diagnosed with a tumour at an advanced stage and that this association had a dose-response effect.(48) Although the reported association is based on the time period immediately before a cancer diagnosis,(48) it still indicates that consulting a GP increases the chance of early detection of cancer.

Patients with low GP consultation frequency are known to have a higher mortality.(43-45) Our findings added new knowledge on the association between usual GP consultation frequency and advanced cancer stage at diagnosis. As the observed association between usual GP consultation frequency and mortality attenuated, but this association remained when we adjusted for tumour stage in the analyses; this clearly

indicates that there is a connection between late-stage diagnosis and increased mortality. Yet, other independent factors, such as a patient's health-care seeking behaviour, seem to play a role.

The patients who did not consult their GP during the 19-36 months before the diagnosis (non-consulters) had a cumulative survival that was 6.1 percentage point lower than the group of patients who consulted the GP three to five times (average consulters) (75.6% vs. 81.7%). This difference applies to 11,567 patients who usually never consulted their GP, which suggests that 706 (20.4%) of the patients who very rarely consulted their GP died prematurely compared to the patients who consulted their GP three to five times. These 706 deaths correspond to 140 deaths annually. This number is not a trivial figure in the Danish setting; it is slightly more than the 120 annual deaths caused by cervical cancer each year in Denmark.(49) Furthermore, the 700 premature deaths account for 2.1% of the observed 33,760 deaths in the present study; this indicates that 2% of all deaths within one year among incident cancer patients in Denmark may be related to low usual consultation frequency in general practice.

The data from this study did not allow us to investigate why these patients had low healthcare seeking. It may be explained by other diseases, e.g. mental illness, which should be elucidated in future research.

Conclusion

In this study, we found an association between low usual consultation frequency in general practice among cancer patients and both higher risk of being diagnosed with distant tumour stage and increased short-term mortality. The association between GP consultation frequency and mortality is a combination of at least two things: a mechanism through more advanced tumour stage and other independent factors. Patients who usually consult their GP rarely may also have delayed help-seeking for cancer symptoms or lower access to healthcare than patients who see their GP on a more regular basis. To develop future interventions that may improve the prognosis for patients with low usual consultation frequency in general practice, the characteristics of these patients should be described and the processes behind their consultation pattern should be explored.

Ethical considerations

The study was approved by the Danish Data Protection Agency (file no. 2009-41-3471). According to Danish law, the study did not require approval from the Committee on Health Research Ethics of the Central Denmark Region as no biomedical intervention was performed. The data that support the findings of this study are stored and maintained electronically at Statistics Denmark. The data are not publicly available due to the Danish legislation on data privacy as the data contains information that could compromise the privacy of the research participants. The data can only be accessed by approved collaborative partners via a secured virtual private network (VPN).

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Conflicts of interests

The authors declare no conflicts of interests.

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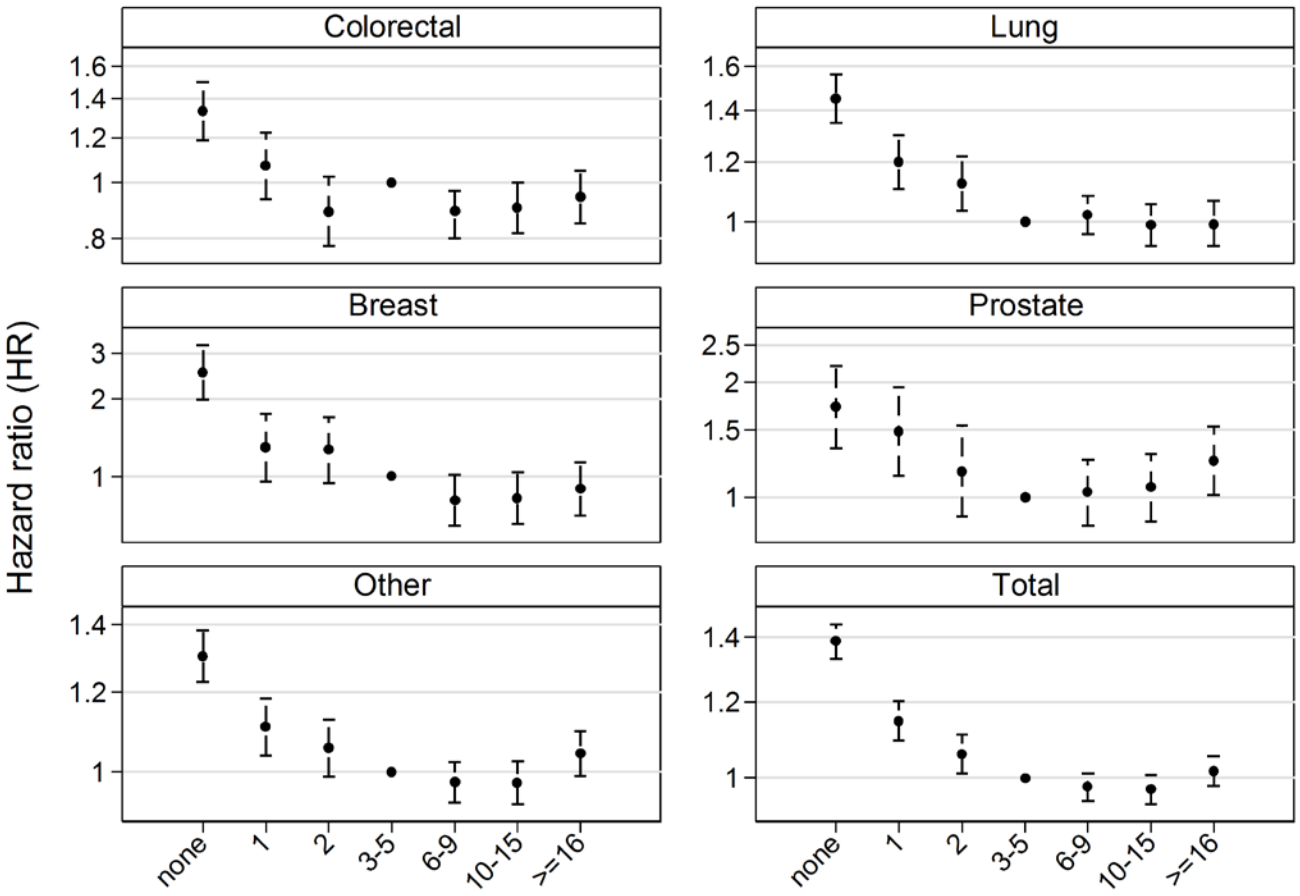

Figure 1: Hazard ratios of dying during the first year after diagnosis according to the number of consultations at a general practice 19-36 months before diagnosis of four cancer types, other types of cancer, and in total. Estimates are adjusted for age, sex, education, income, marital status, and comorbidity.

Table 1: Patient characteristics by cancer site and total (n=123,943).

	Colorectal				Lung				Breast		Prostate		Other				Total					
	Women		Men		Women		Men		Women		Men		Women		Men		Women		Men		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Total	7,853	(45.8)	9,285	(54.2)	8,618	(48.3)	9,243	(51.7)	18,396	(100)	19,348	(100)	23,960	(46.8)	27,240	(53.2)	58,827	(47.5)	65,116	(52.5)	123,943	(100)
Died at one-year follow up	1,855	(23.6)	2,068	(22.3)	4,996	(58.0)	5,920	(64.0)	800	(4.3)	1,036	(5.4)	7,458	(31.1)	9,628	(35.3)	15,109	(25.7)	18,652	(28.6)	33,761	(27.2)
Face-to-face contacts																						
None	672	(8.6)	1,113	(12.0)	633	(7.3)	979	(10.6)	1,512	(8.2)	1,748	(9.0)	1,869	(7.8)	3,041	(11.2)	4,686	(8.0)	6,881	(10.6)	11,567	(9.3)
1	570	(7.3)	794	(8.6)	560	(6.5)	765	(8.3)	1,496	(8.1)	1,645	(8.5)	1,680	(7.0)	2,371	(8.7)	4,306	(7.3)	5,575	(8.6)	9,881	(8.0)
2	611	(7.8)	795	(8.6)	600	(7.0)	696	(7.5)	1,607	(8.7)	1,679	(8.7)	1,786	(7.5)	2,359	(8.7)	4,604	(7.8)	5,529	(8.5)	10,133	(8.2)
3-5	1,791	(22.8)	2,182	(23.5)	1,793	(20.8)	2,040	(22.1)	4,435	(24.1)	4,789	(24.8)	5,350	(22.3)	6,206	(22.8)	13,369	(22.7)	15,217	(23.4)	28,586	(23.1)
6-9	1,829	(23.3)	1,954	(21.0)	2,042	(23.7)	1,971	(21.3)	4,210	(22.9)	4,356	(22.5)	5,538	(23.1)	5,618	(20.6)	13,619	(23.2)	13,899	(21.3)	27,518	(22.2)
10-15	1,330	(16.9)	1,321	(14.2)	1,641	(19.0)	1,522	(16.5)	3,082	(16.8)	3,069	(15.9)	4,345	(18.1)	4,279	(15.7)	10,398	(17.7)	10,191	(15.7)	20,589	(16.6)
≥ 16	1,050	(13.4)	1,126	(12.1)	1,349	(15.7)	1,270	(13.7)	2,054	(11.2)	2,062	(10.7)	3,392	(14.2)	3,366	(12.4)	7,845	(13.3)	7,824	(12.0)	15,669	(12.6)
Tumour stage																						
Local	2,542	(32.4)	3,002	(32.3)	1,703	(19.8)	1,561	(16.9)	10,088	(54.8)	11,154	(57.6)	9,187	(38.3)	9,016	(33.1)	23,520	(40.0)	24,733	(38.0)	48,253	(38.9)
Regional	1,777	(22.6)	2,196	(23.7)	1,591	(18.5)	1,901	(20.6)	5,610	(30.5)	446	(2.3)	1,968	(8.2)	3,066	(11.3)	10,946	(18.6)	7,609	(11.7)	18,555	(15.0)
Distant	1,847	(23.5)	2,185	(23.5)	4,882	(56.6)	5,338	(57.8)	742	(4.0)	1,856	(9.6)	4,058	(16.9)	4,432	(16.3)	11,529	(19.6)	13,811	(21.2)	25,340	(20.4)
Unknown	1,687	(21.5)	1,902	(20.5)	442	(5.1)	443	(4.8)	1,956	(10.6)	5,892	(30.5)	8,747	(36.5)	10,726	(39.4)	12,832	(21.8)	18,963	(29.1)	31,795	(25.7)
Age group (years)																						
50-59	983	(12.5)	1,219	(13.1)	1,434	(16.6)	1,234	(13.4)	5,346	(29.1)	1,982	(10.2)	4,707	(19.6)	5,455	(20.0)	12,470	(21.2)	9,890	(15.2)	22,360	(18.0)
60-69	2,194	(27.9)	3,171	(34.2)	2,926	(34.0)	3,194	(34.6)	7,536	(41.0)	8,099	(41.9)	7,691	(32.1)	10,017	(36.8)	20,347	(34.6)	24,481	(37.6)	44,828	(36.2)
70-79	2,636	(33.6)	3,199	(34.5)	2,925	(33.9)	3,346	(36.2)	3,443	(18.7)	6,829	(35.3)	6,971	(29.1)	7,942	(29.2)	15,975	(27.2)	21,316	(32.7)	37,291	(30.1)
80-89	2,040	(26.0)	1,696	(18.3)	1,333	(15.5)	1,469	(15.9)	2,071	(11.3)	2,438	(12.6)	4,591	(19.2)	3,826	(14.0)	10,035	(17.1)	9,429	(14.5)	19,464	(15.7)
Comorbidity																						
None	6,039	(76.9)	6,657	(71.7)	5,661	(65.7)	5,710	(61.8)	14,923	(81.1)	14,737	(76.2)	18,178	(75.9)	19,186	(70.4)	44,801	(76.2)	46,290	(71,1)	91,091	(73.5)
Moderate	1,527	(19,4)	2,123	(22.9)	2,534	(29.4)	2,806	(30.4)	2,992	(16.3)	3,885	(20.1)	4,825	(20.1)	6,277	(23.0)	11,878	(20.2)	15,091	(23.2)	26,969	(21.8)
High	287	(3.7)	505	(5.4)	423	(4.9)	1,150	(12.4)	481	(2.6)	726	(3.8)	957	(4.0)	1,777	(6.5)	2,148	(3.7)	4,158	(6.4)	6,306	(5.1)
Educational level																						
Basic	4,119	(52.5)	3,435	(37.0)	5,144	(59.7)	4,125	(44.6)	7,379	(40.1)	6,287	(32.5)	11,853	(49.5)	10,059	(36.9)	28,495	(48.4)	23,906	(36,7)	52,401	(42.3)
Short	2,545	(32.4)	4,001	(43.1)	2,527	(29.3)	3,941	(42,6)	6,658	(36.2)	8,305	(42.9)	7,674	(32.0)	11,969	(43.9)	19,404	(33.0)	28,216	(43.3)	47,620	(38.4)
Long	1,189	(15.1)	1,849	(19.9)	947	(11.0)	1,177	(12.7)	4,359	(23.7)	4,756	(24.6)	4,433	(18.5)	5,212	(19.1)	10,928	(18.6)	12,994	(20.0)	23,922	(19.3)
Disposable income																						
Low	3,315	(42.2)	3,037	(32.7)	3,767	(43.7)	3,725	(40.3)	6,152	(33.4)	5,466	(28.3)	9,555	(39.9)	8,437	(31.0)	22,789	(38.7)	20,665	(31,7)	43,454	(35.1)
Intermediate	2,924	(37.2)	2,936	(31.6)	3,447	(40.0)	3,315	(35.9)	6,331	(34.4)	5,606	(29.0)	8,672	(36.2)	8,869	(32.6)	21,374	(36.3)	20,726	(31.8)	42,100	(34.0)
High	1,614	(20.6)	3,312	(35.7)	1,404	(16.3)	2,203	(23.8)	5,912	(32.1)	8,276	(42.8)	5,733	(23.9)	9,934	(36.5)	14,663	(24.9)	23,725	(36.4)	38,388	(31.0)
Marital status																						
Married/partner	3,847	(49.0)	6,467	(69.6)	3,888	(45.1)	5,763	(62.3)	10,805	(58.7)	14,399	(74.4)	12,417	(51.8)	18,067	(66.3)	30,957	(52.6)	44,696	(68.6)	75,653	(61.0)
Divorced/widowed	3,539	(45.1)	2,047	(22.0)	4,229	(49.1)	2,638	(28.5)	6,229	(33.9)	3,712	(19.2)	9,888	(41.3)	6,329	(23.2)	23,885	(40.6)	14,726	(22.6)	38,611	(31.2)
Single/never married	467	(5.9)	771	(8.3)	501	(5.8)	842	(9.1)	1,360	(7.4)	1,237	(6.4)	1,655	(6.9)	2,844	(10.4)	3,983	(6.8)	5,694	(8.7)	9,677	(7.8)

Table 2: Hazard ratios (HRs) for death one year after diagnosis according to number of face-to-face contacts with a GP 19-36 months prior to patient's primary cancer diagnosis.

Face-to-face contacts	Cancer patients	Deaths at 1-year follow-up		HRs and 95% CIs adjusted for age, sex, education, income, marital status, and comorbidity[1]					
				All		Female		Male	
	N	n	(%)	HR	(95%CI)	HR	(95%CI)	HR	(95%CI)
Colorectal (n=17,138)									
None	1,785	436	(24.4)	**1.33**	(1.19;1.50)	**1.41**	(1.18;1.68)	**1.28**	(1.10;1.50)
1	1,364	286	(21.0)	1.07	(0.93;1.22)	1.03	(0.84;1.26)	1.11	(0.92;1.32)
2	1,406	263	(18.7)	0.89	(0.78;1.02)	1.01	(0.83;1.22)	0.80	(0.66;0.97)
3-5	3,973	859	(21.6)	1.00		1.00		1.00	
6-9	3,783	809	(21.4)	0.89	(0.81;0.97)	0.85	(0.74;0.98)	0.90	(0.79;1.03)
10-15	2,651	647	(24.4)	0.90	(0.85;1.00)	0.89	(0.77;1.03)	0.92	(0.80;1.06)
≥ 16	2,176	623	(28.6)	0.94	(0.85;1.05)	0.97	(0.83;1.13)	0.93	(0.80;1.07)
Lung (n=17,861)									
None	1,612	1,105	(68.5)	**1.45**	(1.35;1.56)	**1.38**	(1.22;1.54)	**1.50**	(1.40;1.68)
1	1,325	828	(62.5)	**1.20**	(1.11;1.30)	**1.18**	(1.05;1.34)	**1.21**	(1.09;1.35)
2	1,296	793	(61.2)	**1.12**	(1.04;1.22)	1.10	(0.98;1.24)	**1.14**	(1.02;1.27)
3-5	3,833	2,218	(57.9)	1.00		1.00		1.00	
6-9	4,013	2,414	(60.2)	1.02	(0.96;1.08)	0.99	(0.91;1.09)	1.05	(0.96;1.13)
10-15	3,163	1,906	(60.3)	0.99	(0.93;1.05)	0.96	(0.88;1.05)	1.02	(0.93;1.10)
≥ 16	2,619	1,652	(63.1)	0.99	(0.93;1.07)	0.93	(0.85;1.02)	1.05	(0.96;1.14)
Female Breast (n=18,396)									
None	1,512	112	(7.4)	**2.54**	(1.99;3.24)	**2.54**	(1.99;3.24)		
1	1,496	58	(3.9)	1.30	(0.96;1.76)	1.30	(0.96;1.76)		
2	1,607	62	(3.9)	1.27	(0.95;1.70)	1.27	(0.95;1.70)		
3-5	4,435	161	(3.6)	1.00		1.00			
6-9	4,210	151	(3.6)	0.81	(0.65;1.02)	0.81	(0.65;1.02)		
10-15	3,082	130	(4.2)	0.83	(0.66;1.04)	0.83	(0.66;1.04)		
≥ 16	2,054	126	(6.1)	0.90	(0.71;1.14)	0.90	(0.71;1.14)		
Prostate (n=19,348)									
None	1,748	96	(5.5)	**1.62**	(1.27;2.08)			**1.62**	(1.27;2.08)
1	1,645	77	(4.7)	**1.41**	(1.08;1.83)			**1.41**	(1.08;1.83)
2	1,679	71	(4.2)	1.13	(0.86;1.48)			1.13	(0.86;1.48)
3-5	4,789	188	(3.9)	1.00				1.00	
6-9	4,356	219	(5.0)	1.08	(0.89;1.31)			1.08	(0.89;1.31)
10-15	3,069	190	(6.2)	1.15	(0.94;1.41)			1.15	(0.94;1.41)
≥ 16	2,062	195	(9.5)	**1.44**	(1.18;1.76)			**1.44**	(1.18;1.76)
Other cancers (n=51,200)									
None	4,910	1,693	(34.5)	**1.30**	(1.23;1.38)	**1.32**	(1.20;1.45)	**1.27**	(1.18;1.37)
1	4,051	1,245	(30.7)	**1.11**	(1.04;1.18)	**1.16**	(1.05;1.28)	1.07	(0.98;1.16)
2	4,145	1,208	(29.1)	1.06	(0.99;1.13)	1.03	(0.92;1.14)	1.07	(0.99;1.17)
3-5	11,556	3,510	(30.4)	1.00		1.00		1.00	
6-9	11,156	3,651	(32.7)	0.98	(0.93;1.02)	0.95	(0.89;1.02)	1.00	(0.94;1.07)
10-15	8,624	3,021	(35.0)	0.98	(0.93;1.02)	0.96	(0.89;1.03)	0.99	(0.93;1.06)
≥ 16	6,758	2,758	(40.8)	1.04	(0.99;1.10)	1.01	(0.94;1.09)	**1.07**	(1.00;1.15)
Total (n=123,943)									
none	11,567	3,442	(29.8)	**1.39**	(1.33;1.44)	**1.41**	(1.32;1.50)	**1.36**	(1.30;1.44)
1	9,881	2,494	(25.2)	**1.15**	(1.10;1.20)	**1.16**	(1.08;1.24)	**1.14**	(1.07;1.21)
2	10,133	2,397	(23.7)	**1.06**	(1.01;1.11)	1.05	(0.98;1.13)	**1.06**	(1.00;1.13)
3-5	28,586	6,936	(24.3)	1.00		1.00		1.00	
6-9	27,518	7,244	(26.3)	0.98	(0.95;1.01)	0.94	(0.90;0.99)	1.01	(0.96;1.05)
10-15	20,589	5,894	(28.6)	0.97	(0.94;1.01)	0.94	(0.89;0.99)	1.00	(0.95;1.05)
≥ 16	15,669	5,354	(34.2)	1.02	(0.98;1.06)	0.97	(0.92;1.02)	**1.06**	(1.01;1.12)

Estimates in bold are statistically significant at $p \leq 0.05$ level. [1]In the total analyses, the estimates were also adjusted for cancer type.

Table 3: Odds ratios (ORs) of having distant tumour stage according to number of face-to-face contacts with a GP 19-36 months prior to patient's primary cancer diagnosis compared to 3-5 contacts after multiple imputation of missing tumour stage; displayed by cancer type and total.

Face-to-face contacts	Cancer patients	Distant stage		ORs of having distant tumour stage adjusted for age, sex, education, income, marital status, and comorbidity[1]					
				All		Female		Male	
	N	n[2]	(%)[3]	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
Colorectal									
None	1,785	678	(38.0)	**1.39**	(1.22;1.57)	**1.41**	(1.15;1.74)	**1.36**	(1.16;1.60)
1	1,364	434	(31.8)	1.06	(0.92;1.22)	1.14	(0.92;1.43)	1.00	(0.82;1.21)
2	1,406	483	(34.4)	**1.18**	(1.03;1.36)	**1.34**	(1.09;1.65)	1.07	(0.90;1.28)
3-5	3,973	1,225	(30.8)	1.00		1.00		1.00	
6-9	3,783	1,080	(28.5)	**0.88**	(0.79;0.98)	0.90	(0.77;1.04)	0.87	(0.75;1.00)
10-15	2,651	729	(27.5)	**0.81**	(0.72;0.93)	**0.79**	(0.66;0.95)	0.84	(0.71;1.00)
≥ 16	2,176	546	(25.1)	**0.70**	(0.61;0.80)	**0.73**	(0.60;0.88)	**0.68**	(0.57;0.82)
Lung									
None	1,612	1,097	(68.1)	**1.41**	(1.24;1.60)	**1.47**	(1.20;1.79)	**1.38**	(1.16;1.63)
1	1,325	831	(62.7)	1.10	(0.97;1.26)	1.17	(0.95;1.43)	1.07	(0.90;1.27)
2	1,296	838	(64.7)	**1.20**	(1.05;1.37)	**1.37**	(1.12;1.67)	1.08	(0.90;1.30)
3-5	3,833	2,319	(60.5)	1.00		1.00		1.00	
6-9	4,013	2,418	(60.3)	**0.98**	(0.89;1.08)	0.97	(0.85;1.1)	1.00	(0.88;1.14)
10-15	3,163	1,828	(57.8)	0.88	(0.80;0.97)	0.88	(0.76;1.01)	0.90	(0.78;1.04)
≥ 16	2,619	1,486	(56.7)	0.84	(0.75;0.93)	**0.86**	(0.74;1.00)	**0.82**	(0.71;0.96)
Breast									
None	1,512	177	(11.7)	**3.52**	(2.74;4.53)	**3.52**	(2.74;4.53)		
1	1,496	72	(4.8)	1.35	(0.99;1.85)	1.35	(0.99;1.85)		
2	1,607	75	(4.7)	1.30	(0.95;1.78)	1.30	(0.95;1.78)		
3-5	4,435	177	(4.0)	1.00		1.00			
6-9	4,210	170	(4.0)	0.91	(0.72;1.15)	0.91	(0.72;1.15)		
10-15	3,082	122	(4.0)	0.79	(0.61;1.04)	0.79	(0.61;1.04)		
≥ 16	2,054	84	(4.1)	**0.71**	(0.52;0.95)	**0.71**	(0.52;0.95)		
Prostate									
None	1,748	328	(18.8)	**1.82**	(1.52;2.18)			**1.82**	(1.52;2.18)
1	1,645	267	(16.2)	**1.53**	(1.24;1.88)			**1.53**	(1.24;1.88)
2	1,679	178	(10.6)	0.87	(0.70;1.09)			0.87	(0.70;1.09)
3-5	4,789	588	(12.3)	1.00				1.00	
6-9	4,356	567	(13.0)	0.95	(0.81;1.10)			0.95	(0.81;1.10)
10-15	3,069	438	(14.3)	0.96	(0.82;1.14)			0.96	(0.82;1.14)
≥ 16	2,062	342	(16.6)	0.99	(0.82;1.18)			0.99	(0.82;1.18)
Other									
None	4,910	1,188	(24.2)	**1.28**	(1.17;1.40)	**1.34**	(1.17;1.53)	**1.24**	(1.10;1.39)
1	4,051	857	(21.2)	1.09	(0.98;1.20)	**1.16**	(1.00;1.35)	1.03	(0.90;1.17)
2	4,145	886	(21.4)	**1.10**	(1.00;1.21)	1.10	(0.96;1.27)	1.10	(0.97;1.21)
3-5	11,556	2,368	(20.5)	1.00		1.00		1.00	
6-9	11,156	2,374	(21.3)	1.00	(0.93;1.07)	0.99	(0.89;1.09)	1.01	(0.91;1.11)
10-15	8,624	1,891	(21.9)	0.99	(0.92;1.07)	1.00	(0.90;1.12)	0.99	(0.89;1.09)
≥ 16	6,758	1,522	(22.5)	0.97	(0.90;1.06)	0.99	(0.88;1.11)	0.96	(0.86;1.08)
Total									
None	11,567	3,468	(30.0)	**1.46**	(1.38;1.54)	**1.57**	(1.43;1.72)	**1.40**	(1.30;1.51)
1	9,881	2,461	(24.9)	**1.14**	(1.07;1.22)	**1.72**	(1.06;1.29)	**1.12**	(1.03;1.23)
2	10,133	2,460	(24.3)	**1.11**	(1.05;1.18)	**1.21**	(1.10;1.32)	1.05	(0.97;1.14)
3-5	28,586	6,676	(23.4)	1.00		1.00		1.00	
6-9	27,518	6,609	(24.0)	0.96	(0.92;1.01)	0.95	(0.89;1.02)	0.97	(0.91;1.04)
10-15	20,589	5,008	(24.3)	**0.92**	(0.88;0.97)	**0.91**	(0.84;0.97)	0.94	(0.88;1.01)
≥ 16	15,669	3,980	(25.4)	**0.88**	(0.83;0.93)	**0.87**	(0.81;0.94)	**0.89**	(0.82;0.96)

Estimates in bold are statistically significant at p≤0.05 level. [1]In the total analyses, estimates were also adjusted for cancer type. [2]Estimated from the proportion derived from multiple imputation. [3]Percentage of distant cancers out of number of cases in face-to-face group.